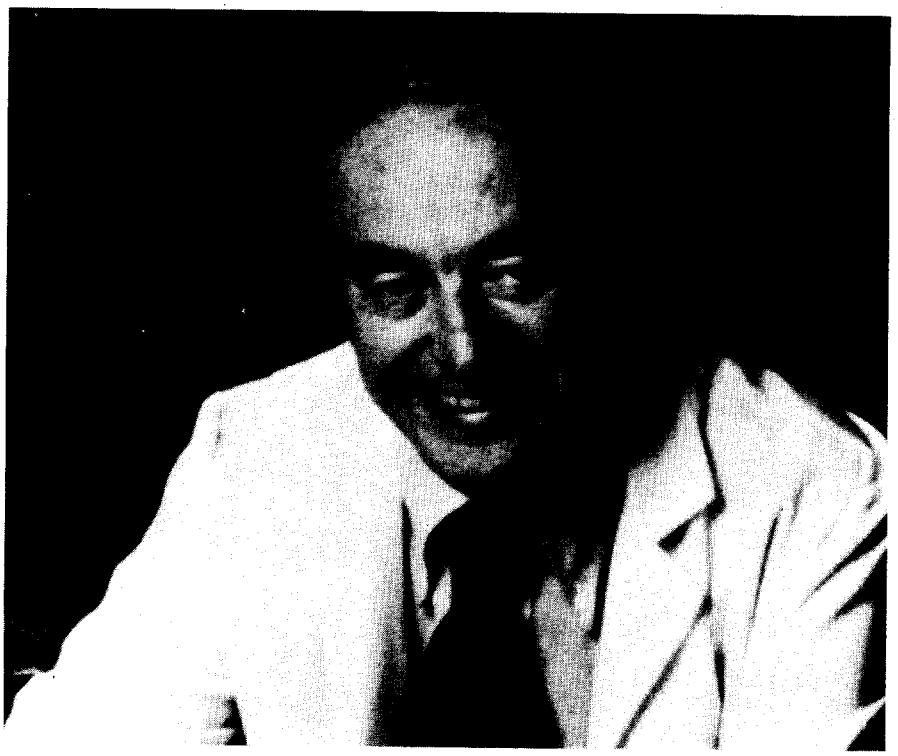
An interview with Edward D. Freis, MD, on:

Pharmacologic and behavioral strategies in treating hypertension



What type of hypertensive patient should receive an individualized treatment regimen?

Are there significant differences in cardiovascular mortality rates between hypertensives on pharmacologic regimens, and controls?

In what areas are behavioral techniques most effective in hypertension management?

What are some practical preventive measures that can be taken against developing hypertension?

Behavioral Medicine: What is your view on the recent study by the Hypertension Detection and Follow-Up Program (HDFP)? Did you find any new clinical implications that will be of service in the management of the disease?

Freis: The HDFP was not designed as a controlled clinical trial to specifically answer the question of the effectiveness of antihypertensive drug treatment in preventing cardiovascular complications. It was instead intended to be a comparison of the effectiveness of total care as delivered in special hypertension clinics (SC group) versus another group who were referred to whatever community medical services that were available including private practitioners (RC group). Thus, the RC patients cannot be regarded as an untreated control group. Many of the RC patients received treatment before the end of the study. The average diastolic blood pressure of the RC group was reduced to 90 mm Hg. as compared to 85 mm Hg. for the SC group. Blood pressure, therefore, was reduced in both groups although it was greater in the SC group by a decrement of 5 mm Hg. diastolic pressure. Therefore, the results of the study with respect to effectiveness of drug treatment, *per se*, must be regarded as *suggestive* rather than *conclusive*.

While not conclusive, the HDFP study provides further suggestive evidence that treatment is beneficial in preventing cardiovascular complications in patients with mild (diastolic 90-104 mm Hg.) hypertension. Most other studies also suggest this conclusion. The original Veterans

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Administration study, for example, indicated a 40 percent lower incidence of major cardiovascular complications in the drug treated patients as compared to the placebo group. However, the number of patients in the trial was too small for this difference to obtain statistical significance. Similar favorable trends also were found for the prevention of all cardiovascular complications (but not myocardial infarction alone) in the 90-100 mm Hg. group of patients who were in the Australian trial. Again, however, the differences were not statistically significant. A preliminary report of the Society of Actuaries provides additional suggestive evidence that treatment of mild hypertension is protective. Taking all of the available evidence into consideration the trend is favorable toward concluding that treatment is effective in mild hypertension, even though no study provides definitive evidence. The requirement of large numbers in order to demonstrate a significant difference between treated and control patients indicates that the difference probably is small. Even in the highly favorable HDFP study the 5 year cardiovascular mortality was approximately 4.4 percent in the RC and 3.3 percent in the SC patients. The difference in mortality, therefore, was only 1.1 percent over 5 years. This is not a great difference and it should give us pause before committing the 35 or more million persons with borderline or mild hypertension to life long treatment.

Behavioral Medicine: Then you have some reservations about advocating long-term pharmacologic approaches to managing mild hypertension?

Freis: Because of the above uncertainties the course that has seemed wisest to me is to individualize the care of patients with mild hypertension. I try to select those in the 90-99 diastolic range who are at highest risk and treat them, while those at lowest risk would be followed but not actively treated. Patients at highest risk are those of young age, male or black, with a family history of severe hypertensive complications and with evidence of target organ disease such as left ventricular hypertrophy in the electrocardiogram. Additional factors increasing the risk of myocardial infarction are cigarette smoking, hypercholesteremia and diabetes mellitus.

The outlook of a 55-year-old white woman with no other risk factors than a blood pressure of 155/92 mm Hg. is near that of a normotensive individual. It is questionable that treatment will provide any prolongation of useful life in such a patient. Furthermore, the expense and inconveniences of treatment could be considerable. On the other hand, a 35-year-old male with a blood pressure in the same range but with a strong family history of hypertension and with electrocardiographic evidence of left ventricular hypertrophy should receive treatment.

The HDFP has brought us further evidence in favor of treatment. The evidence, however, is not conclusive. We await a more complete analysis of their findings and also that from other studies such as the Australian trial and the British Medical Research Council Trial which is still in progress. In the meantime, this observer at least will individualize patients with mild hypertension for treatment.

Behavioral Medicine: How effective do you feel behavioral techniques are in managing hypertension?

Freis: Behavioral techniques can modify the blood pressure, but in my experience their effect is fairly transient. Again, research in this field has been hampered by lack of adequate controls. Blood pressure tends to drift down over weeks or months of observation without any treatment. This has been frequently noted in the placebo group of controlled clinical trials. The downward drift of blood pressure is probably due to a progressive loss of apprehension as the patients become more acclimated to the clinic and feel more at home there. This downward drift can be mistaken for a therapeutic effect of behavioral or other techniques unless a control group is followed along concurrently.

Relaxation exercises, transcendental meditation and the like lower blood pressure for the period that the patient is relaxing. In my opinion these are all methods for decreasing the activity of the sympathetic nervous system and this causes the fall in blood pressure. However, once the patient assumes his normal wakeful life the sympathetic nervous system will again become active and the blood pressure will rise to its former level. I do not believe, therefore, that behavioral techniques permanently modify hypertension or represent a practical approach toward its long term treatment.

Behavioral Medicine: Are there any circumstances under which you would recommend some types of behavioral strategies to help encourage hypertensives to become more involved in their treatment? What kinds of strategies might you use?

Freis: The most frequently encountered major problem in treatment is noncompliance. To facilitate the regular taking of medications the patient's customary behavior must be modified. First the patient should be instructed in the nature of the hypertension and why its control is important to his or her future welfare. To facilitate pill taking we have the patient obtain a compartmented pill box which represents each day

of the week. The pill box is filled by the patient with the supply of tablets for each day of the week. It is then placed in a prominent position on the bathroom sink so that the patient is certain to see it during the customary ablutions of the morning and night.

This is only part of a larger program aimed at making the patient conscious of the fact that it is he and he alone who is ultimately responsible for the success of his treatment.

Behavioral Medicine: This problem of patient compliance with regard to drug therapy is a major concern for physicians. Often the side effects discourage patients from continuing treatment. What other suggestions do you have for practitioners in combating this problem?

Freis: The physician should be alert to the fact that the patient may be having discomforting side effects that he or she does not want to talk about such as, in male patients, sexual impotence. Truly disturbing side effects that persist require attention if the cooperation of the patient is to be maintained. The dose of the offending drug may need to be reduced or if necessary discontinued with substitution of another antihypertensive agent.

Behavioral Medicine: Taking into account the need to minimize side-effects which may lead to noncompliance, what pharmacologic regimens would you recommend?

Freis: Noncompliance is caused not only by side effects but also by the number of drugs and the frequency of dosage. The drug regimens which can be given as one tablet, once per day have an inherent advantage over regimens that involve several different kinds of tablets given 3 or 4 times per day so far as compliance is concerned. Most of the antihypertensive medications on the market today have a low incidence of side effects. Therefore, I am not willing to recommend one regimen over another. There is tremendous variation in responsiveness from one patient to another with respect to individual drugs. Therefore, I prescribe a simple one tablet per day regimen first and change to a more complicated regimen only if side effects require it.

Another basic principle in minimizing side effects is to begin treatment with a small dose of the antihypertensive agent and increase the dose gradually. By this means side effects if they occur will be less severe than if the patient was given full doses of the drug initially.

Behavioral Medicine: What type of treatment program would be needed to treat hypertension that is refractory to the commonly prescribed antihypertensives?

Freis: The first point to try to settle is whether the resistance to treatment is due to poor compliance. Careful questioning of the patient and checking with the pharmacist as to the frequency of prescription refills are some of the techniques used to determine compliance.

Another point to check is whether the patient has had an adequate response to the diuretic. In patients with renal impairment (serum creatinine 3.0 mg/100 ml or higher) the patient may not achieve a satisfactory diuresis from the customary thiazide diuretics. In such cases doses of 80 mg or more of furosemide are needed to achieve a diuresis. Once that is obtained the patient usually will become responsive to antihypertensive drugs again.

If the patient remains refractory despite an adequate diuresis and he has received a trial of the standard antihypertensive agents such as a beta adrenergic blocking agent, alphamethyldopa or clonidine along with diuretic and hydralazine, the following course may be taken. If the patient is below age 45 a work-up for secondary forms of hypertension should be carried out. If the patient has severe hypertension he should be treated with minoxidil.

Behavioral Medicine: The manner in which an individual reacts to environmental stress, and perceives his or her experiences, can have a profound effect on blood pressure levels, especially when the person "angers-in" or silently seethes with hostility. Do you feel some form of psychotherapy, such as the cognitive approach, can help to some degree in the management of essential hypertension?

Freis: I do not believe that psychotherapy has proved to be an effective approach to the treatment of hypertension. There is no question, however, that stress raises blood pressure temporarily while the individual is in a state of emotional excitement. So far as stress is avoidable the patient should try to do so.

Behavioral Medicine: How can the primary care physician help his or her patients in the prevention of hypertension?

Freis: Hypertension probably could be prevented if the individual ate a diet extremely low in sodium. By that I mean a diet containing about 1 gm or less of salt per day. This is impractical, however, because such a low sodium diet is not feasible in our society.

The most practical and useful preventive measure is to avoid weight gain. Obestiy is strongly associated with hypertension and reduction in weight in obese hypertensives lowers the blood pressure to normal. However, the most important preventive factor is to pick the right parents because inheritance plays the largest role in the genesis of essential hypertension. ■